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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/605,266	06/28/2000	Rama Akella	SBI-066	6018
7590 03/09/2004				
KENNETH S. BARROW CENTERPULSE USA INC. 12E. GREENWAY PLAZA SUITE 1000 HOUSTON, TX 77046-1203		EXAMINER ANDRES, JANET L		
		ART UNIT		PAPER NUMBER
		1646		

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/605,266

**Applicant(s)**

AKELLA ET AL.

**Examiner**

Janet L. Andres

**Art Unit**

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-24 and 26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 and 18-23 is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-17, 24, 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 5/2003.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **RESPONSE TO AMENDMENT**

1. Applicant's amendment filed 12 December 2003 is acknowledged. Claims 1-24 and 26 are pending and under examination. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

#### ***Claim Rejections/Objections Withdrawn***

2. The objection to claim 25 is withdrawn in response to Applicant's cancellation of this claim.
3. The objection to claim 24 is withdrawn in response to Applicant's amendment correcting the claimed subject matter.
4. The objection to claims 6 and 18-23 as depending from a rejected claim but being otherwise allowable is withdrawn in response to Applicant's amendment incorporating the limitations of claim 1 into claim 6 and of claim 13 into claim 18.

#### ***Claim Rejections Maintained/ New Grounds of Rejection***

5. The rejection of claims 9-12 under 35 U.S.C. 102(b) as anticipated by the '739 patent is maintained for reasons of record in the office action of 5 May 2003.

Applicant has amended the claims to require that the mixture be treated to remove histones, and further require that at least one growth factor must maintain native post-translational modifications. Applicant argues that it would not be reasonable to conclude that combining proteins as taught by the '739 patent would result in exactly the same mixture as that now claimed.

Applicant's arguments have been fully considered but have not been found to be persuasive. The '739 patent teaches the two proteins claimed and teaches both synthetic and

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recombinant forms. Treatment of the proteins to remove histones or ribosomes would not result in a mixture that differed from proteins that were already free of histones or ribosomes. The proteins would be precisely the same. Recombinant proteins can have, and preferably do have, native post-translational modifications. A combination of BMP-2, BMP-3, and TGF- $\beta$ 2, as specifically taught by the '739 patent, recombinantly produced in a mammalian cell using techniques pointed to by the '739 patent in column 6, lines 4-25, which paragraph refers to standard works teaching such techniques, would be a combination comprising BMP-3 and TGF- $\beta$ 2 that was free of both histones and ribosomes and maintained native post-translational modifications.

6. The rejection of claims 1, 3-5, 7, and 8 under 35 U.S.C. 103(a) as unpatentable over the '406 patent in view of EP 0 433 225 A1 is maintained for reasons of record in the office action of 5 May 2003.

Applicant has amended claim 1 to require that the mixture be bone derived and treated to deplete histones. Applicant argues that the mixture that would result from a combination of the '406 patent with EP 0 433 225 A1 would not have been subjected to such treatment. Applicant has amended claim 3 to require that any additional growth factors be in their native post-translationally modified form. Applicant argues that neither reference suggests that either growth factor be phosphorylated or glycosylated.

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated above, proteins produced recombinantly in mammalian cells would meet the limitations of these claims. They would be free of histones or ribosomes and would inherently be in their native modified form. The origin of the proteins and whether they are free

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of histones or ribosomes because of their means of production or because they have been treated does not change that nature of the proteins themselves. What is encompassed by Applicant's claims are mixtures of proteins that are free of histones or ribosomes and maintain native post-translational modifications. Recombinantly produced mixtures would have those characteristics.

See *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985):

The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

7. The rejection of claim 2 under 35 U.S.C. 103(a) as unpatentable over the '406 patent in view of EP 0 433 225 A1 and further in view of Stelnicki et al. is maintained for reasons of record in the office action of 5 May 2003.

Applicant has amended the claims as set forth above and has amended claim 2 to require that any additional growth factor be in its native form. Applicant argues that the cited references do not teach or set forth such combinations.

Applicant's arguments have been fully considered but, for the reasons set forth in paragraphs 5 and 6 above, have not been found to be persuasive. The nature of the compositions remains the same, regardless of their means of production.

8. The rejection of claim 24 under 35 U.S.C. 103(a) as unpatentable over the '739 patent in view of EP 0 433 225 A1 and further in view of the '490 patent is maintained for reasons of record in the office action of 5 May 2003.

Applicant argues as set forth above, that the combined references would not provide a product that had been treated to remove ribosomes.

Applicant's arguments have been fully considered but have not been found to be persuasive. For the reasons set forth in paragraphs 5-7 above, the added limitation does not change the nature of the final product.

9. The rejection of claims 13-17 under 35 U.S.C. 103(a) as unpatentable over the '328 patent in view of the '739 patent, the '483 patent, and Ksander et al. is maintained for reasons of record in the office action of 5 May 2003.

Applicant has amended the claims to require that the mixtures be bone derived and treated to remove histones and/or ribosomes, and that they maintain their native modifications. Applicant argues that the mixture resulting from the combination of these references would not necessarily have been treated and would not necessarily maintain post-translational modifications.

Applicant's arguments have been fully considered but have not been found to be persuasive. For the reasons set forth in paragraphs 5-8 above, proteins having the properties that would result from the treatments of the instant claims are disclosed in the references.

10. Claim 26 is newly rejected under 35 U.S.C. 102(b) as anticipated by U.S. patents 5563124, 5371191, and 5290763, of record in the office actions of 13 August 2002 and 11 February 2002.

These patents teach the mixture of figure 1 and its use in for treatment of bone growth. Such a use would inherently promote angiogenesis, regardless of whether that property was recognized at the time or not.


CLAIMS 6 AND 18-23 ARE ALLOWED. CLAIMS 1-5, 7-17, 24 AND 26 ARE REJECTED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday-Thursday and every other Friday, 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.  
5 March 2004



JANET ANDRES  
PATENT EXAMINER